GUIDELINES FOR

THE REGISTRATION AND CONTROL OF PESTICIDES

FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS

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COMMUNITY

GUIDELINES FOR THE REGISTRATION

AND CONTROL OF PESTICIDES

(including a model scheme for the establishment of national organizations)

FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS

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1. INTRODUCTION

Despite improved farming practices in many countries, including the application of fertilizers and pesticides, world food production has barely kept pace with the expanding population this century, and half of the world's population today has an inadequate diet. Food supplies will have to be doubled in the next 30 years to achieve even a moderate advance in nutritional standards. The World Food Conference in 1974 recognized that a greatly increased use of fertilizers and pesticides is among the measures essential for achieving the massive expansion needed in food production.

Pests destroy up to one-third of the world's food crops during growth, harvesting and storage. In developing countries crop losses are even higher. Quite apart from all this, agriculture is the world's major industry, over 50 percent of the wrold's population being dependent upon agriculture for its livelihood.

In the highly inter-related, inter-dependent world of modern technology and trade, the challenge of protecting crops and livestock from insects, diseases, weeds, and other pests without hazard to people, animals or their environment requires the combined and sustained efforts of scientists, technicians, and administrators; of producers, processors, and distributors; of industry and government; and of nations working together to establish and administer sound, acceptable standards of food safety and environmental quality.

The wholesomeness of any food supply depends in part on the quality of the total environment: the soil, water, and air in which the food is grown, processed, and consumed. Acute contamination of these basic natural resources by pesticide residues and other pollutants can affect not only the safety of food products, but also other environmental values such as water supplies, wildlife preservation, and outdoor recreation. Nations are actively seeking to protect and manage these resources in the interests of greater safety and human welfare.

Most nations are committed by law, policy and traditions to assuring their constituents that their food supply is adequate, safe, clean, and wholesome. In order to give effect to such laws and policies it is necessary to develop criteria and protocols that are effective and workable. It should be the objective to achieve these goals with minimum dislocation of production or trade, but under no circumstances should adverse affects on people or the environment be countenanced to serve economic goals. While pesticides are intended to effectively control organisms that destroy or endanger man's food, health or environment, under some circumstances and at concentrations above a certain threshold, they, like virtually every chemical, may have physiological effects on other organisms living in the environment, including man himself. Whether the effects occur or not is simply a question of the dosage and of proper use.

Hand in hand with the increasing complexity, potency and applications of chemicals designed to control unwanted animal and plant life has developed an increasing but understandable concern about the safety of these chemicals to users, livestock, wildlife, the environment, and especially to consumers of foods produced with their assistance.

This public concern has made it necessary for governments to review the standards and procedures for evaluation and acceptance of new pesticides prior to sale. A system, involving registration, has evolved and, under increasing pressures, has become increasingly stringent, diverse and more responsible.

The term "registration" used in this context should not be confused with the registration of a motor vehicle or a trade mark. In each of these cases the procedure simply involves the recording in a register of a few salient details which establish ownership, evidence of which is then provided by a

document for which the registrant pays a designated fee. Such operation entails the minimum of time, expense or documentation. In the case of pesticides, registration follows the evaluation and acceptance by a Statutory Authority of extensive documented proof submitted in support of all claims for efficacy and safety made for the proposed product. Registration implies a number of different controls among which evaluation is the most important. For a pesticide to be adequately assessed for registration purposes extensive scientific information must be developed by the manufacturer on many aspects of the product, particularly its properties and performance.

The purpose of registration is to ensure that pesticides, when used according to registered label directions, will be effective and efficient for the purposes claimed, and safe. Misused, pesticides can certainly be harmful. Properly handled, they form an essential management tool in the production of food and fibre.

This, then, is the reason for registration: to allow availability of suitable pesticides and to ensure proper, effective, safe use.

Many countries, especially those with highly developed technologies, have therefore set up regulatory procedures to control trade practices and the production and use of pesticides.

The elaborate regulatory procedures of developed countries are strengthened by a comprehensive enforcement system. Such a system and the regulatory procedures it is designed to enforce make demands on available resources which developing countries will often find impossible to meet.

However, developing countries need not introduce elaborate regulatory schemes in order to control pesticides effectively. The innovative process leading to the introduction of new pesticides has hitherto been limited to a number of technologically advanced countries where the basic laboratory work (toxicology, chemistry, environmental studies, analytical methodology, etc.) can be done, and where the results of such work are evaluated as part of the regulatory procedure. Once evaluated, those results are valid world-wide and may be considered transferable. Developing countries can therefore use such data as inputs, without having to produce them independently.

Once a country has decided that some measure of control of pesticides is desirable and feasible it will need to determine the extent of the resources and effort which can be put into the system of control and which aspects should receive priority.

Developing countries should design regulatory procedures suited to their specific needs, and not attempt to adopt all the elements of regulatory schemes used in developed countries. The standards for acceptance of a pesticide in one country, such as an industrial food-exporting country with a temperate climate, an abundance of fertile land available and advanced agricultural technology, would not necessarily be applied in another country with different agricultural practices, a different climate or economy.

The use of a pesticide should be permitted only if the benefits outweigh the risks involved. The balance between risk and benefit will differ greatly under different socio-economic conditions and it is important for each country to study its own priorities when deciding which compounds may be used. It should not be influenced too much by decisions made elsewhere. For example, in a country with a highly developed system of agriculture and adequate resources the threat of harm to a rare bird species may be sufficient reason to avoid the use of a particular compound, whereas in situations where vector-borne human diseases, starvation and malnutrition are regularly encountered, the risk/benefit analysis is likely to result in a different decision.

2. THE NEED FOR CONTROL OF PESTICIDES

One of the prerequisites of a pesticide is that it should be effective in the control of the target organisms when applied in a convenient manner at a pre-determined rate. Unfortunately, few pesticides possess a high degree of specificity. Most of them are toxic to non-target organisms as well as to target organisms and they therefore carry a potential health hazard to the person who handles them as well as to the consumers of treated crops. They may also, of course, have adverse affects on wildlife. Because of their potential toxicity to non-target organisms, they may have far-reaching effects on man and wildlife and the public therefore demands effective control over their availability and use.

How best to reduce the hazards of pesticides to man and animals is a problem that has occupied many individuals and organizations the world over. In electing to control the introduction of pesticides through some type of registration scheme national authorities have been mindful of the needs of the many inter-related and inter-dependent segments of the community. The following needs must be considered:

Users. Farmers, householders and other end-users are concerned with the effectiveness, efficiency and any hazards associated with use. They are concerned to know how much to use, when to use it, how to apply it and how to ensure that they get best value for their investment. They need clear instructions, adequate directions for use and appropriate stimulus to observe any limitations and any precautions necessary for the protection of themselves, others or the environment.

The General Public. Children, neighbours, bystanders, and persons transporting and storing pesticides are concerned with such hazards as accidental poisoning, spillage, and safe handling, storage and disposal. Their needs must be considered since they can readily become innocent victims of other people's carelessness or inadvertent actions.

Consumers. In countries with an advanced agriculture each farmer may produce sufficient food for many people who may live far away - even overseas. The safety of food is a paramount concern to both public and public health authorities who demand that food should contain the least possible amount of chemical residue and that there is evidence by which to judge that such residue is without hazard to consumers.

Crop and Plants. The vulnerability of crops being treated necessitates careful consideration of the phytotoxicity of each and every chemical. The possibility of non-target species being affected by spray drift, run-off, carry-over in soil or contamination of spray machinery necessitates most careful evaluation and adequate precautions.

Livestock and Domestic Animals. Because of high economic and sentimental value such animals need protection from adverse effects of pesticides irrespective of whether the compounds are directly applied, applied to animal feeding stuffs, or to their environment. The susceptibility of some species of animals to individual pesticides may be quite high and the need for adequate precautions must be determined in advance.

The Environment. The need to safeguard the environment from adverse effects of pesticides is widely recognized. Contamination of air, soil, water and waterways should be avoided wherever possible. The potential hazard to wildlife, non-target insects and other ecological components must be minimized.

Vendors. Those who market pesticides need to be protected from false or unfair claims from competitive products.

Manufacturers. Manufacturers who develop, formulate, pack and market pesticides need an adequate standard by which they and others may judge the suitability of products for the market place. There is strong support for legislation which protects reputable manufacturers from unreasonable and unfair competition from inferior, unsafe, or untested products.

Trade. Local and overseas trade in manufactured pesticides needs the stabilizing influence of adequate legislation, reasonable standards and the knowledge that each will be judged for compliance with these standards. Because of the importance of trade in agricultural commodities including food, fibre and industrial commodities, trading partners and national authorities need assurance that the availability and use of pesticides is regulated to avoid, as far as possible, contamination of these commodities with residues above acceptable limits.

A well-devised and operated system for regulating the introduction and availability of pesticides and for controlling such aspects as formulation quality, packaging, labelling, storage and methods of application will go a long way towards preventing ill effects from pesticides. However, education, dissemination of information, particularly on correct usage, disposal of surplus materials and empty containers and treatment in the case of accidents, is of paramount importance if full benefit is to follow the introduction of a registration scheme.

The advantages which can follow the registration of pesticides depend, of course, on the extent of the controls exercised. Insistence of accurate and informative labels will be of benefit to manufacturers, formulators and repackers, as well as to those using the products. Independent assessment of efficiency claims and safety will reassure the vendor and farmer and the general public will be more confident about the use of products deemed by the authorities to be safe for the user, the consumer and the environment.

2.1 Objectives

The goal in regulating pesticides is to provide society with adequate protection from adverse effects while not denying it access to benefits from their use.

The principal method of establishing the manner in which a pesticide may be marketed and used is through the registration requirements. There are potential problems with pesticide usage but the purpose of the large amount of research going into the generation of data for registration is to tackle the issues before they become problems.

Registration enables authorities to exercise control over quality, use levels, claims, labelling, packaging and advertising and thus to ensure that the interests of end-users are well protected. The registration legislation must provide a system under which the public's interest and the manufacturer's rights are protected.

If every pesticide has to be registered the public will know at a glance that the product on sale has satisfied the requirements of the law as to its effectiveness and safety when used according to the directions on the label. This qualification is important but necessary, as no regulatory agency can guarantee against misuse.

2.2 Responsibilities

There are four levels of responsibility associated with the registration of pesticides:

Manufacturers. The prime responsibility rests with the manufacturer who must first be satisfied that the product fulfils the many requirements demanded by the public and the government authorities charged to watch the public interest. The manufacturer must ensure that there is adequate

scientific evidence to support all claims for efficacy and safety. It is not generally recognized that registration authorities do not usually ask questions more difficult than or different from those demanded by corporate management or those charged with research and development responsibilities for new pesticides.

The manufacturer must be satisfied that he has generated sufficient scientific information to effectively and positively answer at least the following questions:

- Is it effective?
- Is it efficient?
- Is it reliable?
- Is it adequately stable?
- Is it safe to users?
- Is it safe to bystanders?
- Is it safe to consumers?
- Is it safe to crops?
- Is it safe to livestock?
- Is it safe to wildlife?
- Is it safe to beneficial organisms?
- Is it acceptable for the environment?
- Will it present problems in trade?

Implicit in these questions are many issues and aspects which the manufacturer must consider and on which appropriate scientific data must be forthcoming. If and when all this information is available the manufacturer may approach regulatory authorities in confident expectation that they will judge the data adequate and acceptable.

Governments. In most countries it is recognized that a period has been entered characterized both by a fuller understanding of the risks and advantages of pesticides and a desire to provide adequate controls, either voluntary or mandatory, to ensure that the use of pesticides does not adversely affect public health, beneficial organisms, the environment or trade. Government policy must be aimed at protecting the public and the environment from excessive exposure to harmful substances while also preserving and increasing the great variety and utility of products that have contributed so much to the improvement of our food supply, protection of our health, the increase in trade and the standard of life.

Governments should establish legislation to regulate the manufacture, sale and use of pesticides. Such legislation must be based on regulations that establish a permissible safe use pattern for each chemical. This use pattern must be described on the labelling for each product and the labels need Government approval. In addition, safe legal limits should be established for residues in food and feed.

Some countries exercise control over both safety in use and efficacy while others control only one or the other. In some countries, the protection of the operator stops with the label directions, but in others, the law imposes responsibility on employers in respect of their employees. Many countries make use of the idea of an experimental permit, temporary clearance or licensing to allow new pesticides to be field tested and some registration authorities undertake a critical laboratory and field examination of new products.

In summary, the objectives of Government are to:

- protect the unwary from the unscrupulous;
- prevent unsubstantiated claims;
- ensure adequate directions for use;
- highlight precautions and limitations in use;
- protect the uninitiated from his own ignorance;

- safeguard reputable manufacturers from spurious claims by disgruntled users;
- engender confidence in the system by the general public.

Vendors. Those engaged in the distribution and sale of pesticide products carry a heavy responsibility to ensure that they do not offer for sale products which are not registered and that they do not promote uses which are not recommended on approved labels. Users rely heavily upon their suppliers for guidance in the safe and effective use of pesticides and it is recognized that such sales outlets provide the major source of information reaching users. Because of this, the role of supplier carries with it both privilege and responsibility.

Users. Users must recognize the responsibility to themselves, their families, their neighbours, the community, the environment and those who might ultimately consume the produce grown with the aid of pesticides.

The directions on registered labels have been developed at great cost in time, money and scientific manpower, have been evaluated by experienced scientists and have been approved by Government Authorities. The claims and directions are made in the knowledge that if they are followed the result will be satisfactory and there will be no untoward hazard. Unless users accept their responsibility and see that the directions on registered labels are followed carefully and conscientiously, the efforts of manufacturers and governments will have been to no avail.

3. DESIGNING A REGULATORY SCHEME

In designing a regulatory procedure the first step must be to define the subject matter. A useful definition of a pesticide is as follows:

> Pesticide - Any substance or mixture of substances intended for preventing, destroying, or controlling any pest, including unwanted species of plants or animals during the production, processing, storage, transport, or marketing of food, agricultural commodities or animal feedstuffs or which may be administered to animals for the control of insects, arachnids or other pests in or on their bodies. The term includes substances intended for use as a plant-growth regulator, defoliant, desiccant or fruit thinning agent or agent preventing the premature fall of fruit and substances applied to crops either before or shortly after harvest to protect the commodity from deterioration during storage and transport. The term excludes fertilizers or their plant nutrients and agents such as veterinary medicines and feed additives administered to animals for other purposes such as to stimulate their growth or to modify their reproductive behaviour and substances added during processing of food.

The next step is to decide on the form of regulatory procedure, taking all the above definition into account. There are several possibilities, including the following:

(a) Voluntary scheme. No legal force would be required with such a scheme, under which regulation is based on mutual trust and understanding. There must be some guarantee, however, that the scheme cannot be undermined by non-participants;

(b) Preventive scheme. In principle, it would be forbidden to produce, import, sell, use or otherwise dispose of pesticides, unless explicitly allowed. When properly enforced, such a scheme is practically foolproof, but it involves considerable bureaucratic procedures and resources;

(c) Retrospective scheme. Within the framework of a set of basic rules, there would be no freedom to produce, sell, use or otherwise dispose of pesticides, but companies and individuals would be held responsible and called to account for what they did or neglected to do if mishaps occurred. Such a system is much simpler to operate, but has the great drawback that action will usually be taken only after an incident has occurred. Moreover, it pre-supposes a certain level of education and sense of responsibility of everyone concerned;

(d) Government scheme. Only the Government or bodies empowered by it would be allowed to produce, import, sell, use or otherwise dispose of pesticides. The drawbacks of the scheme are that it involves considerable bureaucracy and limits individual initiative;

(e) Regional scheme. Under such a scheme, two or more countries of similar agricultural and political background would have a common regulatory procedure and share use of resources.

The final decision on a regulatory scheme will have to be based primarily on an assessment of the agricultural and economic structure of the country, but legislative and political factors will also play a role in most cases.

It is important to make a careful assessment of the enforcement potential. As has been stated above, the real value of a regulatory procedure is largely dependent on the practicability of enforcing it.

It is absolutely vital that adequate care is taken in determining which authority should be responsible for designing, operating and enforcing the regulatory procedure.

Given the largely agricultural use of pesticides, the most appropriate authority would normally be the Minister of Agriculture. However, since aspects of the protection of public health, the environment and the economy are also involved, the ministers and executive authorities responsible for those fields should also have a role to play.

Once it has been determined under which ministry the prime responsibility for the regulatory procedure should fall, one person should be appointed, together with a staff, to bear the daily responsibility. Such an executive will henceforth be called the "Registrar of Pesticides" or "Director of Pesticide Registration".

Expert help is available (e.g. from FAO) to assist in these decisions and consultation at an early stage can prevent costly mistakes, and delays in the initiation of a scheme.

4. PESTICIDE LAWS

Legal powers will be necessary for effective control of pesticides. They should apply to import, sale, labelling, application, storage and disposal of surplus technical grade active ingredients and formulations other than those intended solely for export and which are prepared and packed according to the specifications or directions of a foreign purchase. If already in existing legislation covering other chemical products, manufacturing, repacking and transport do not need to be brought within the pesticides law as the risks they present are similar to those of other chemical products and are, therefore, presumably already covered by appropriate legislation.

The law should state that no person or corporate body should distribute, sell, offer for sale or deliver within or import into the country a pesticide or product containing pesticide unless:

(1) it has been registered with and assigned a registration number by the appropriate authorities, or

(2) it is covered by a trials or provisional clearance from the authorities for use in accordance with the conditions stipulated in that clearance.

The law should specify the warning signs and symbols to be included on labels of products depending on their toxicological category, the precautions to be taken when applying these products and the way in which they should be labelled, used, packed and stored.

The procedure for obtaining registration should be prescribed in detail by regulations made under the pesticide legislation. Data supplied by the applicant for registration and submitted in confidence should be treated as administratively confidential and specific to the application under consideration.

The authorities may, after considering the data, accept the product for registration, issue a provisional permit or reject the application. Registration may be suspended, cancelled or modified at any time if new data become available which shows it should be reviewed.

Applicants should be informed of the reasons for such rejections, suspensions, cancellations or modifications, which should be subject to appeal within periods fixed by regulations made under the pesticide legislation.

Any printed or graphic material relating to and accompanying the product should conform to the labelling requirements and advertisements and similar material must not make claims outside the terms of the registration. It should be unlawful for any person to:

(1) supply a product unless it bears a label conforming to the regulations;

(2) supply a product which has decomposed or deteriorated so as to be ineffective or dangerous, or is in containers which have deteriorated or been damaged so as to be dangerous in storage or use;

(3) detach, alter, deface or destroy any label on the container of a product in a manner which may defeat the purpose of the pesticide legislation;

(4) add any substance to a product labelled in accordance with the pesticide legislation;

(5) repack or transfer the contents of a pesticide product container unless (a) the new containers bear labels conforming to the pesticide regulations and (b) the repacking is carried out under supervision and any necessary precautions (e.g. wearing protective clothing) are observed;

(6) to advertise any product in a manner that is false, misleading and deceptive or not justified by the conditions of its registration.

Regulations may contain special provisions with regard to substances or operations which present a high or unusual degree of hazard and may, for example, prescribe conditions for field evaluation of experimental compounds or restrict the sale of specified substances to ensure their use only by certain categories of persons. They may, also, make any provisions concerning marketing or use that may be necessary to safeguard third parties, the environment and wildlife resources other than such noxious plants and animals whose control is desired.

One of the keys of the success of any pesticide registration scheme for the official control of pesticides hinges on cooperation between agricultural and health officials. Before any registration scheme can be satisfactorily introduced, full and comprehensive discussions should be held with officials from both ministries. The continuing success of the scheme depends on frank discussions and cooperation being maintained at all times. Before any pesticide can be used or recommended by agricultural authorities, the chemical must be cleared by the health experts.

There are six main areas where coordination is essential:

(1) in the formulation of regulations to control pesticides;

(2) in the training of medical personnel and agricultural inspectors in the treatment of pesticide poisoning and safety aspects of application;

(3) in the training of users;

(4) giving of practical advice on protective measures;

(5) in determining whether, in the light of experience, use of certain pesticides should be restricted;

(6) in the setting of standard procedures for residue analysis, MRL's and preharvest intervals.

It is also obviously very important that adequate instruction should be available in the use and application of the particular pesticide once the correct target has been identified.

Since neither of the parties associated with the safe and effective use of pesticides can exert adequate control on their own, systems of coordination must be worked out.

5. IMMEDIATE CONTROL OF PESTICIDES

The establishment of an effective pesticide registration scheme may take several years. Countries which do not have any controls over the import, manufacture or sale of pesticides may want to control the availability of highly toxic and perhaps ineffective pesticides. These countries may not have the resources immediately available to develop a pesticide registration scheme and in these cases it is suggested that an immediate measure to control pesticides along the following lines could be implemented. However, in the long term control of pesticides by an effective registration scheme is the preferred measure.

(1) Determine kinds of pesticides available and their major uses through market surveys, discussions with industry representatives and extension workers.

(2) Write to pesticide registration directors in countries with similar climatic and socio-economic conditions for information on availability/restriction/prohibition of Class Ia and Ib pesticides.

(3) Discuss with directors of Customs, Trade and Industry, Health, and Legal Department to determine simple means of control.

(4) Draw up a proposed schedule of pesticides which will be restricted (indicate manner of restriction) or prohibited.

(5) Discuss proposed schedule with extension workers and industry representatives.

(6) Gazette proposed schedule to come into force in about 6 months' time under appropriate existing laws stating that pesticides in the schedule can only be imported, manufactured, formulated, packed, repacked or stored for sale in accordance with the stipulation in the schedule.

6. PLANNING THE ESTABLISHMENT OF A REGULATORY ORGANIZATION

Any level of resource available can be usefully employed. An indication of the suitability of products for various uses may be obtained by a study of the lists of products that are permitted in countries having a comprehensive registration scheme provided that the reasons for omission from such lists is understood. This is most important because the absence of a pesticide may be due to circumstances particular to a country such as the development of resistance or the availability of a more effective, but expensive, alternative. The use of the latter may be justified in one country, but uneconomic in another where a lower level of pest control is acceptable. Similarly, possible side effects, such as harm to birds, may be considered more undesirable in one country than in another.

Where no laboratory facilities are available contract laboratories can be used to assess the quality of formulations and to determine residues in crops, maximum residue limits for which are published by the Joint FAO/WHO Codex Alimentarius Commission (2). However, the regulatory control which can be exercised with such limited facilities is most unlikely to be adequate and within a short time the introduction of a more comprehensive system for the registration of pesticides will be seen to be highly desirable.

A registration scheme should apply to all pesticides with the exception of those used for the control of internal parasites of humans, livestock and pets, the regulation of which is usually the concern of the medical and veterinary authorities. Thus it should apply to use in agriculture, animal husbandry, horticulture, forestry, public health, food storage, on ships, in warehouses, in shops, for the control of pests in and around the home, etc., and allowance should be made for new and unforeseen uses of pesticides which may be introduced at any time.

Coordination between the various government departments is essential so that all aspects relating to pesticides can be controlled centrally by one comprehensive process. As pesticides are indispensable to modern agriculture they already form an important part of the work of agricultural departments. Moreover, departments of agriculture, through their advisory extension officers, have an established contact with the most prolific users of pesticides. For these reasons, registration schemes are usually administered by a section within the department of agriculture.

In many countries the agricultural department may be concerned with evaluating the need for pesticides in particular crops or areas and should provide independent and authoritative advice to those growing and storing crops concerning the most appropriate pesticide, application rate, time, etc. The health department, although primarily interested in the public health use of pesticides, should assess, often with the occupational health department, the toxicity of all pesticide formulations to establish if and how they can be used without harming those applying or handling them or consuming treated crops. It also must liaise with the medical profession on methods of treating any poisoning cases. The department of the environment is concerned with the possibility of any undesirable side effects such as killing of wild life beneficial to agricultural production (e.g. pollinating insects) or used as food (fish) or for amenity reasons. The departments of trade and transport have to deal with all types of merchandise, including hazardous chemicals but, provided these authorities are supplied with appropriate information, it is unlikely that pesticides will present them with any particular difficulties in making appropriate determinations.

The organization to which the responsibility for administering a registration scheme is assigned needs sufficient legal powers to ensure that:

(1) all products are submitted for registration;

(2) adequate data are provided to enable a decision to be made on whether, to what extent and under what conditions the product may be used, effectively and safely;

(3) only registered products are offered for sale;

(4) products are used only in the approved manner.

Petitions for the registration of products are submitted by industry and, as both government and industry have essential roles to play in a successful and effective registration scheme, relations between them should be cordial, harmonious and founded on mutual trust. Governments must be confident that the evidence submitted is reliable and that all relevant facts have been reported to them. Industry must feel that it is being treated fairly and that there are no unwarranted delays.

Within the registration organization there must be access to suitable expert advice and adequate facilities for the evaluation of the submitted data. To obtain greatest benefit the organization should be able to publish its decisions in the form of lists of registered (approved) pesticides as well as advice to those involved in agriculture, food storage, etc. and to implement programmes to train people in the correct use of pesticides.

In a later section of this paper a plan is given for the phased introduction of a registration scheme over a period of 7-8 years. Although a definite order of expansion is suggested, it is recognized that this will not necessarily be ideal for all countries. The point at which a country enters the plan and the extent to which it progresses and the rate of progress through the various stages will depend on the needs of the country and the level of its financial, scientific and administrative resources. If, for example, the most important action needed is the removal from the market of products which are ineffective, it may be considered desirable to bring forward the appointment of a biologist to carry out trials to compare the various products. Similarly, if the services of a competent contract laboratory are available, it may be possible to delay, or even omit, the appointment of a residue chemist. Further, an assessment of existing facilities may show that some of them could be extended or modified to produce the necessary data.

When a conclusion is reached on the actions which are necessary for the introduction of a registration scheme an overall plan should be made and responsibilities for its constituent parts firmly allocated. Any unavoidable delays or unforeseen difficulties should be reported to the coordinator so that any necessary modifications can be made to the rest of the plan.

For the smooth introduction of a comprehensive scheme for the registration of pesticides it is important to plan carefully the various operations involved. Apart from passing the necessary legislation and the appointment and training of a pesticide registration director, the timing of certain other actions, which need to be started early, can be critical. Amongst these are the designing, building and equipping of laboratories for the testing of formulations and the determination of residues. Sufficient time must also be allowed for the appointment and training of chemists and their assistants. Some of this training, and that of the registar, is likely to involve visits to countries where registration schemes are already well established and time must be allowed for these to be arranged and to take place.

The following bar chart, covering a period of 8 years, gives suggested timing for the initiation and completion of various actions. It is recognized that the plan contains elements of both the idealistic and the practical. It will depend on the resources available to the country. If the plan can be achieved, it should be possible by the end of the period to have:

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(1) issued registration certificates for those products which were on sale prior to the start of the registration scheme and which have been shown to be effective and without unacceptable hazard;

(2) published a list of registered products for the guidance of users;

(3) tested for quality many, if not most, of the pesticide formulations on the market;

(4) informed the sellers of existing products which have not been registered of the reasons for withholding registration and indicated what additional data are needed for a final decision or why it was felt that registration of the product was unjustified;

(5) issued guidelines on correct labelling, storage and disposal of unwanted pesticides;

(6) prevented the import of unregistered products;

(7) established the facilities available to determine pesticide residues in foodstuffs grown under commercial conditions;

(8) established the facilities to carry out field evaluations to assess efficacy of products.

6.1 Explanation of the Bar Chart

Actions 1-2 should be initated as soon as it is decided to introduce a pesticide registration procedure. It will be necessary beforehand to establish the number and type of formulations being sold. Once these facts are known, a decision can be made on the extent to which pesticides need to be controlled and a suitable law enacted. This should, at least, prohibit after a specified date the import, sale or use of unregistered pesticides.

Actions 3 to 4 concern the appointment, training and functions of the pesticides registration director (PRD - see section 6.2) and his officers. A minimum of six months is likely to be needed for training and to establish good working relationships with specialist biologists, toxicologists, etc.

Action 5 concerns the establishment of a Board which is comprised of technically qualified senior officers of relevant departments including Health Department, Forestry, Environment, Standards Institute, and other government agricultural agencies. In addition to the technical personnel from departments, a suitably qualified alternate from each agency should be appointed to attend meetings in the absence of the head of department. Non-government agencies are usually not represented on the Board, although this should be left to Governments to decide. The Board will establish policy and general direction in the regulation of pesticides.

Action 6 concerns the establishment of a small temporary laboratory in an existing building for the qualitative and quantitative analysis of active ingredients in major pesticides. It must be emphasized that compromise must not be made with regard to laboratory safety.

Action 7 calls for the Board to issue protocols for registrion data and labelling requirements.

Actions 8-9 concern the designing, building, equipping and staffing of laboratories which will provide facilities for the analysis of products and for checking residue levels in crops when grown commercially. Allowance should be made preferably for overseas training of chemists.

Action 10 calls for an assessment of products already on the market.

Actions 11-16, 17-18, and 19-20 concern the appointment and training of product chemists, biologists and toxicologists who will directly assist the PRD in the evaluation of applications for registration in their respective fields and also ensure that the labels contain the necessary and correct information.

Action 21 is publishing a list of registered products.

PLAN FOR ESTABLISHING A REGISTRATION ORGANIZATION

Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7	Year 8
1. Prepare & Pass Bill							
	2. Prepare and gazette Registration Rules						
3. Appoint Pesticide Registration Director		4. Train PRD					
	5. Board Established and Functioning						
6. Build temporary laboratory	7. Instructions on registration data, labelling & hazard classification issued						
8.		Plan and Build Permanent Laboratory					
	9. Obtain Laboratory Equipment & Reagents						
		10. Assessment of Existing Products					
11. Appoint & Train Product Chemists							
	12. Start up Product Lab. & obtain equipment for residue lab.		13. Check Quality of Formulations				
	14. Appoint and Train Residue Chemist	15. Start up Residue Lab.	16. Check Residue Levels				
17. Appoint & Train Biologists		18. Carry out Field Evaluation and Assess Bioefficacy Data					
19. Appoint and Train Toxicologists		20. Assess Toxicological Data					
						21. List of Registered Products Published	

As a priority, products already on the market should be tested so that those of inferior quality can be improved or denied registration. This will give some assurance that the purhcaser will get value for money. Later, new formulations being submitted for registration should have to pass a quality control test as part of the registration process.

It is important to be able to assess human and environmental hazards which could arise from residues of pesticides in foodstuffs, water, etc. In addition, certain important export crops must be analyzed to ensure that exports are not jeopardized due to presence of excessive pesticide residues. When the residue laboratory is equipped, staffed and functioning efficiently, its initial task should be to analyse food samples grown commercially, i.e., using a standard schedule of pesticide treatments.

6.2 The Pesticides Registration Director (PRD)

This is the key position and the success of the registration scheme, particularly in the early stages, depends on the appointment of a suitable person. The director should be a scientist who is also a good administrator and who has an interest or background in agriculture. It is desirable that he should have some knowledge of chemistry, botany, entomology, plant physiology, ecology and mammalian toxicology, but as all this knowledge is unlikely to be found in one person, time must be allowed for training him to a standard at which he can commence operations. As he gains experience and has contact with specialists in other disciplines he ought to obtain a knowledge of all the disciplines, sufficient to enable him to understand the advice he is given and to be able to appreciate the importance of the information contained in the registration petitions submitted to him. It is desirable that good relationships are established as soon as possible with any (or the most important) government biological and toxicological research stations and that the PRD has access to official publications from such bodies as FAO, WHO and several countries with well-established registration schemes. He will need the use of a technical library and would be very much helped by subscribing to one of the specialized abstracting services; this could postpone, or even make unnecessary, the establishment of an index of toxicological, residue and other data. He needs the means to publish lists of registered products and advice on the safe use of pesticides.

6.3 Technical Committees

The Board may from time to time establish one or more technical committees to look into specific problems and to provide recommendations. It is essential that members of such technical committees should comprise the PRD, his relevant officers and officials from other government agencies and universities who may be knowledgeable on the subject.

6.4 Enforcement

The value to be derived from an efficiently administered control scheme eventually depends on the practical implementation and enforcement of the laws. Powers must be given to the registration authorities to cancel a registration if it is felt that the continued registration poses undue risk to users, the environment or the general public. A product should also be de-registered if the applicant had flouted the law with regard to active ingredient content, labelling requirements, etc. It would, however, be prudent to first of all allow the applicant to show cause why the registration should not be cancelled; this should then be considered by the Board and appropriate action taken.

In countries where pesticides are being registered for the first time, adequate publicity should be given of the coming into force of the registration requirements. Pesticide retailers ought to be given about a year to dispose of old stocks of unregistered pesticides.

Nevertheless, several inspectors should be appointed who should in good time visit all pesticide retailers in the country and provide published information on the enforcement of the laws. After period of grace is over, enforcement officers should enter premises manufacturing, storing or selling unregistered pesticides and seize all such pesticides and bring to book the offenders. In the case of imports of unregistered pesticides, close collaboration should be maintained with the Department of Customs and action be taken against importers of unregistered pesticides.

6.5 Assessment of Registration Petition

Countries vary in the expertise available for the assessment of registration petitions in general and the toxicity sections in particular. There is often, in addition, a shortage of laboratory facilities for checking quality and performance of new pesticides. These difficulties are especially acute before a pesticide registration scheme has been introduced and in the first few years of its operation. They may be at least partially overcome by:

(1) Including amongst the requirements for registration a list of countries where the active ingredient and/or the proposed formulation has been registered together with proof of registration. Registration certificates usually specify the crop(s) on which the product may be used, the application rate and interval between treatment and harvest. Some reassurance on the suitability and safety of the material may be gained by the number and extent of registrations granted but, more valuably, by the significance of the countries which have granted registration; information on registrations in countries with comparable climates and crops are particularly valuable.

(2) In the early stages of the development of pesticides few or perhaps no registrations may have been granted at the time a registration authority is asked for permission to import the pesticide. If, within the country, there is a shortage of suitable trained experts to assess the data submitted, it may be possible to seek the views of an international organization such as FAO or employ a consultant. If the data sumitted are inadequate, a stepwise approach may be made to the registration so that the amount of the product which may be used and the variety of crops treated are restricted to the extent of the evidence. As further data become available the nature, number and extent of permitted uses can be increased. If the authorities are in doubt about any pesticide, views can be obtained from international organizations such as the International Register of Potentially Toxic Chemicals (IRPTC) or the International Program for Chemical Safety (IPCS).

(3) Concentrating available resources on the careful and detailed consideration of the draft label and the scientific information that bears directly on each aspect of the label (see Section 9, Labelling). Refer to the FAO Guidelines on Pesticide Labelling for detailed help (3).

7. PHASED REGISTRATION

Phased, or as it sometimes may be called, stepwise registration procedures for pesticides have been in operation in a number of countries for some time. Such procedures have many advantages, both for the regulatory authority and for the manufacturer, in that they enable all parties to verify that the results of the laboratory or small scale trials are achieved in the field following wider use and thus allows any necessary modification to be made to the registration proposals before a full commercial registration is issued.

The development of a pesticide is a gradual but complex process. It is reasonable for the authority to allow the pesticide to be used in accordance with limitations or restrictions imposed by the regulatory authority during this development provided there is no undue risk to operators, the public or the environment.

During the phased registration stages, additional data that are required to enable both the authority and the manufacturer to evaluate the efficacy and possible side effects of the pesticide and to decide what additional testing, if any, may be necessary. It would be unrealistic to expect manufacturers to be able to provide the complete dossier to any registration authority before a submission could be considered.

In some instances, the chemical may be withdrawn by the manufacturer before registration is finalized due to difficulties which have come to light during the phased registration process. A phased registration system enables an evaluation of the performance of the product in the hands of farmers to be undertaken and observations on wildlife to be made from wide, but supervised, use.

By proceeding slowly there is a greater chance that all parties will be more fully aware of any problems arising from the application of the pesticide. However, there is no need for it to be a requirement that all chemicals must proceed through a phased registration system. For example, a product based on an active ingredient which has been in use for many years, may be granted registration immediately, subject, of course, to the provision of acceptable data.

However, as a general principle, it is suggested that all products based on new active ingredients should proceed through a phased system so that full evaluations of new pesticides are undertaken before registration is granted and unrestricted marketing commences.

7.1 Phases in the Registration Process

Provided an initial set of basic data is available then limited registration should be considered. There are three clearly identifiable stages in the development of a pesticide.

Trials (or experimental) Clearance: This would normally be granted for a period of one year. The trials would be supervised or monitored and the extent of such trials may be confined to a specific maximum. Generally the food or feed harvested from such trials would not be permitted to be used although in some instances permission to utilize it may be given. After the specified period of clearance, renewal could be granted, but before this the manufacturer would need to show that although some work has been done on the development of the product and more is still required.

Provisional (or limited) Clearance: This type of clearance could be granted when most of the relevant registration data have been obtained. Some data, because of their very nature, can only be obtained when the scale of use of the pesticide is sufficient to demonstrate a measurable effect (or lack of one) on operators or on the ecology of the treated area. At this stage the product could be sold, but usually sales would be restricted to a certain quantity, perhaps over a specified period.

Commercial (or full) Registration: This would be granted after a thorough evaluation of all data showed that the pesticide could be used without unacceptable risks. Registration authorities may, however, restrict the claims, place limitations on use, place a time limit on the tenure of the registration, or review any situation at any time in the light of new evidence. It should be emphasized that any registration is always subject to review in the light of new information coming to hand.

7.2 Data Required for Different Phases

It is not the intention to provide "check lists" for the various phases of registration as the check list concept should not be used in the registration process. Data supplied in support of registration must be able to be utilized and it is definitely not recommended that data be requested just for the sake of having it on the file. It is basic to the concept of phased registration that a lesser amount of data would be required at the trials clearance stage than would be required at a more advanced stage in the process. The amount of data required at the various stages of clearances will vary depending on the nature of the pesticide and the proposed use. The following guidance is provided to assist in judging what would seem to be reasonable requirements for data. These data requirements are set out under five main headings, that is, chemical and physical properties, toxicology, environmental, residues and efficacy. Suggestions are made concerning use limitations and labelling which should be considered at each of the clearance stages.

7.3 Amount of Data Required and Suggested Limitations for Trials Clearance

The amount of data required at this stage of clearance will be quite minimal because of the limitations that the product will not normally be able to be sold, but will be for use only by bona fide research workers. Because the product is not for sale it will usually not be necessary for the regulatory authority to place a quantity limit on the amount to be used in trials. However, the manufacturer should specify the amount required for trials work so that the regulatory authority is aware of what is being used and can, if appropriate, suggest a reduction in the quantity permitted. At this stage minimal labelling requirements would be adequate.

7.3.1 Chemical and Physical Properties: Chemical name, common name and/or code number, formulation, simple physical and chemical properties (if available).

7.3.2 Toxicology: An indication of the toxicity, i.e. LD50 figures plus first aid precautions to be followed in the event of accidental poisoning.

7.3.3 Environmental: Some data may be needed to indicate the possible effect on desirable species, depending on the proposed use regime. In most instances this may be predicted from the chemical and physical properties. Refer to FAO Guideline on Environmental Criteria for the Registration of Pesticides (20).

7.3.4 Residues: There will usually be no local data and thus it should be a general requirement that treated crops be not fed to animals or humans, and animals be not allowed to graze treated areas. From proposed use patterns, and knowledge of the chemical supplemented by any available residue data it may be possible for authorities to be confident that residues at harvest or grazing will not pose a hazard. Thus the general restriction against consumption could be waived. Refer to FAO Guidelines on Crop Residue Data (18).

7.3.5 Efficacy: No local data will be available, but there will be an indication from the manufacturer's screening tests of the likely effect on the pest spectrum. The application should define the pest(s) against which evaluation is intended and the amount of product to be used for trials. Refer to FAO Guideline on Efficacy Data for the Registration of Pesticides for Plant Protection (15).

7.3.6 Limitations: Limitations at this stage would be that the product will not be for sale, and will be for use only be research workers employed by government, universities or the manufacturer.

The trials permit should be issued for a specific period of time, usually one year, which could be extended on request.

7.3.7 Labelling: At this stage a typewritten label will be acceptable, provided it contains information on the chemical type, precautions to take when handling the pesticide, together with an indication of the pests and situations where the product will be tested.

7.4 Amount of Data Required and Suggested Limitations for Provisional Clearance

This is an important stage in the phased registration process in that it will give the manufacturer and the regulatory authority the opportunity to see whether the results of the small scale tests carried out under the trials clearance phase are achieved under a wide range of conditions. A considerable amount of data is required for provisional clearance. At this clearance stage, the product can be sold and it is therefore important that residue data obtained during trials clearance be provided so that maximum residue limits can be established, if appropriate, where the product is used on food crops. Usually a limit would be placed on the amount of product which can be sold and also a time over which such clearance would be valid. Full labelling is required.

7.4.1 Chemical and Physical Properties: Chemical and physical properties of the technical grade active ingredients, and the formulated product should be provided. While there could be some situations where something less than the complete data could be sufficient, generally speaking as much as possible should be submitted. See pages 22-24 of this document.

7.4.2 Toxicology: The amount of toxicological data required for provisional clearance may vary markedly from country to country, with some countries requiring the full package and others a somewhat lesser amount. The final decisions on how much data to require must be left to the registration authority, but as a guide at least information from short term and subacute studies should be provided. Long-term animal studies may not be required before provisional clearance is granted, provided it is made clear that such studies must be completed and submitted before full registration will be considered. The decision as to whether long-term studies are required at provisional clearance level will also be influenced by the nature and proposed use of the chemical. See pages 25-26 of this document.

7.4.3 Environmental: The primary data needed for predicting environmental hazards are:

(1) the properties of the pesticide including chemical and physical properties, biological, metabolism and residue studies; and toxicological information; and

(2) the influence of use patterns which takes into account formulation, methods of application, site, time and type of application, scale of use and the climatic and geographic locality.

The registration authority should be able to make a good prediction of the environmental hazards following assessment of the above data. Where such predictions indicate a possible hazard for specific components of the environment, further specified data will need to be collected during the period of provisional clearance. Refer to FAO Guidelines on Environmental Criteria for the Registration of Pesticides (20).

7.4.4 Residues: Residue data from tests conducted under trials clearance must be provided when the proposed use of the pesticide may lead to the creation of residues in food or feed. These data must have been obtained from supervised trials following use according to proposed label claims. Guidelines for the design and layout of residue trials have been developed by the Codex Committee on Pesticide Residues and the Commission on Pesticide Chemistry of the International Union of Pure and Applied Chemistry and published by FAO (4), IUPAC (5) and GIFAP (6) following a recommendation from the 1977 ad hoc Consultation. These guidelines discuss trial design, sampling techniques, packaging of samples and reporting of results. It may be necessary for the appropriate authority to set a maximum residue limit either on a temporary or a firm basis to permit the sale of treated produce. Residue data developed in accordance with the above guidelines will be a necessary part of this evaluation. Refer to FAO Guidelines on Crop Residue Data (18).

7.4.5 Efficacy: Reports on trials carried out under trials clearance must be presented to show that the chemical will control the pest organism without adversely affecting the crops. Such trial results should demonstrate the effect on crop yields, and crop quality, selective varietal differences as well as compatibility with other chemicals and with agricultural practice. The results should:

(1) demonstrate the effect on the pest organism;

(2) measure the reliability or consistency of control;

(3) provide information on the duration of control;

(4) define limitations including safety to crop, animal or substrate being treated;

(5) show a comparison with the standard product or practice normally used;

(6) determine, where applicable, the effect of variables such as temperature, moisture, and soil on effect of the pesticide on the pest organism.

Details of studies of efficacy and crop safety which should be reported and submitted to the registration authority are to be found on page 24. Refer to FAO Guidelines on Efficacy Data for the Registration of Pesticides (15).

7.4.6 Limitations: It is normal for the regulatory authority to impose a restriction on the amount of pesticide which can be sold under provisional clearance. The authority should stipulate the period of time during which the clearance shall remain valid. The provisional clearance should lapse unless any additional data required to support full registration is provided.

7.4.7 Labelling: As the pesticide is to be sold, full details as to identification, precautions, and directions for use and storage should be on the label which should generally comply with the FAO Guidelines on Good Labelling Practice for Pesticides (3).

7.5 Amount of Data Required and Suggested Limitations for Full Registration

7.5.1 Chemical and Physical Properties: Any additional data, e.g. modification to formulations, should be provided. Also details on ways of disposal of unwanted material and containers should be provided plus any additional information as may be required by the authority. See pages 22 to 24 of this document.

7.5.2 Toxicology: Any outstanding tests (for example, the results of any long-term testing not available at time of provisional clearance) must be made available. See pages 26-27 of this document.

7.5.3 Environmental: Reports of observations made during the wider use of the pesticide showing any effects on fish or other wildlife should be provided. If, for example, the primary data showed that the chemical has a high toxicity to birds, then special attention would be given to the possibility of adverse effects during use under provisional clearance and these data would be required before registration is granted. If a pesticide is intended to be used in or close to water or on rice, toxicity tests on fish and fish food organisms should be carried out. Likewise, additional data on other possible environmental hazards such as leaching through the soil or effects on soil organisms following use under provisional clearance and in accordance with proposed use patterns may be required. Refer to FAO Guidelines on Environmental Criteria for the Registration of Pesticides (20).

7.5.4 Residues: Generally little additional data would be required as maximum residue limits would have normally been set and/or acceptable waiting periods (withholding periods or pre-harvest intervals) established prior to provisional clearance having been given. Residue monitoring data should be provided if available. Refer to FAO Guidelines on Crop Residue Data (18).

7.5.5 Efficacy: Additional data will usually be of a qualitative rather than a quantitative nature with possible major emphasis being placed on observations on phytotoxicity or fruit finish following wider field usage. Refer to FAO Guidelines on Efficacy Data for the Registration of Pesticides for Plant Protection (15).

7.5.6 Limitations: Registration may be granted for a set period or for an undefined time depending on the requirements of the authority granting registration, but parties must be aware that in the event of new knowledge about the pesticide coming to hand it may be necessary to review registration at any time.

7.5.7 Labelling: Full labelling as for provisional clearance plus details on the disposal of containers, disposal of unwanted or contaminated product. The use of standard phrases for all precautionary labelling is recommended. Refer to FAO Guidelines on Good Labelling Practice for Pesticides (3).

8. DETAILED INFORMATION REQUIRED FOR REGISTRATION

The amount of data which must be supplied by those seeking registration will depend mainly on the extent of the registration required. If only small quantities of the material are to be used in trials which will be carried out by trained personnel wearing protective clothing and on crops which are to be destroyed or used for residue determinations very little information will need to be supplied. (See Trials Clearance, Section 7.3).

Conversely, if the petitioner wishes to market unlimited quantities for use on a staple diet crop, a very complete dossier of information will be necessary to enable an evaluation to be made of the efficacy and potential hazard of the product. A relaxation in the requirements is appropriate for compounds which have been used for many years without apparent ill effects and where it is known that, when used properly, they produce residues below the permitted limits. In this chapter guidance is given on the extent of the data which may need to be supplied for the evaluation of a typical new pesticide. An explanation of the relevance of some types of information to the assessment of the suitability of pesticides is provided.

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8.1 Detailed Data on Chemical and Physical Properties

In order to define a pesticide chemical, it is imperative to have clear, accurate and precise details of its chemical and physical properties in terms that can be measured. To this end, pesticide manufacturers are required to supply to registration authorities comprehensive data on those physical and chemical characteristics which are identifiable and determinable and to make a declaration of the composition of the pesticide.

Information is required on the physical and chemical properties and purity of the technical grade material used in the formulation as well as on the formulated product itself. Further precise information on the properties and characteristics of the active ingredient are usually needed for control purposes.

In addition, it is usual to include certain data that are used in other aspects of hazard evaluations of a pesticide (for example: partition co-efficent water/n-octanol can often be used to assist in the estimation of the bio-accumulation potential of a compound).

Analytical methods for the determination of the active ingredient and impurities in the technical and formulated product are an essential part of the information required. Where standardized or published methods are not available, details of an appropriate method must be provided by the manufacturer.

This information is needed to define the composition of the technical grade active ingredient in the product registered. It is implicit that the toxicological, residues and efficacy studies submitted in support of a registration have been carried out with material of comparable composition. It is also presumed that the registrant will ensure that the marketed product complies with the compositional statement made at the time of registration.

Some of the descriptive characteristics and certain properties which influence mobility and degradation of a pesticide are obviously important in predicting its environmental behaviour.

In the control of the marketed pesticide, it is important that certain criteria of identity, quality and reasonable performance should be identified and selected from the physical and chemical properties. Such a selection may then form the basis of a specification. Internationally agreed specifications for many pesticides are available from FAO (7) and WHO (8) and these should be consulted when a petition for registration of any such pesticide is under consideration.

The basic data related to the active ingredient and the commercial product should include, when appropriate:

ACTIVE INGREDIENT

1. Identity

   1.1 common name proposed or accepted by ISO and synonyms;
   1.2 structural formula;
   1.3 chemical name (according to internationally agreed nomenclature, preferably IUPAC);
   1.4 empirical formula and molecular weight;
   1.5 manufacturer's development code number(s);

2. Physical Properties of the Pure Active Ingredient

   2.1 appearance (physical state, colour, odour);
   2.2 melting/decompostion/boiling point;

2.3 vapour pressure (figures should be given at a stated temperature preferably in the range of 20-25°C), but only when above 10-3 Pascal);
2.4 solubility in water and organic solvents (at a stated temperature preferably in the range of 20-25°C);

2.5 partition coefficent between water and an appropriate non-miscible solvent (e.g. n-octanol);
2.6 density (for liquids only);
2.7 hydrolysis rate under stated relevant conditions;
2.8 photolysis under stated relevant conditions;
2.9 absorption spectra, e.g. ultra-violet, visible, infra-red, etc.

3. Technical Grade Active Ingredient

3.1 source; name and address of manufacturer and addresses where manufactured;
3.2 appearance (physical state, colour and odour);
3.3 the minimum (and maximum) active ingredient content in g/kg;
3.4 identity and amount of isomers, impurities and other by-products, together with information on their possible range expressed as g/kg.

FORMULATED PRODUCT

1. General Description (Identity) of the Formulated Product

In addition to the information required for the active ingredient, the general description of the formulated product to be registered should, in all cases, include:

1.1 formulator's name and address;
1.2 distinguishing name (proprietary name);
1.3 use category (herbicide, insecticide, etc.);
1.4 type of formulation (water dispersible powder, emulsifiable concentrate, etc.).

2. Composition

2.1 content of technical grade active ingredient(s) (where more than one active ingredient, information should be given on each ingredient separately);
2.2 content and nature (identify if possible) of other components included in the formulation, e.g., technical grade, adjuvants and inert components;
2.3 water content (where relevant).

3. Physical/Chemical Properties of the Formulated Product

3.1 appearance;
3.2 storage stability (in respect to composition and physical properties related to use);
3.3 density (for liquids only);
3.4 flammability: liquids - flashpoint; solids - a statement must be made as to whether the product is flammable;
3.5 acidity (where relevant);
3.6 alkalinity (where relevant);
3.7 other properties may in certain cases need evaluation.

4. Physical Properties of the Formulated Product Related to Use

The following list is not exhaustive for either properties or types of formulation. Some relevant test methods may be found in CIPAC Publications (26), but other proven methods may also be used.

4.1 wettability (for dispersible powders);
4.2 persistent foam (for formulations applied in water;
4.3 suspensibility (for dispersible powders and suspension concentrates);
4.4 wet sieve test (for dispersible powders, suspension concentrates);
4.5 dry sieve test (for granules, dusts);
4.6 emulsion stability (for emulsifiable concentrates);
4.7 corrosiveness (when necessary);
4.8 known incompatibilities with other products, e.g., pesticides, fertilizers. Refer to FAO Guidelines on Specifications (7).

8.2 Detailed Data on Efficacy

The pests, diseases and weeds of major food crops and pests of significance to public health continue to be controlled by the use of chemical pesticides which offer, in many cases, the only satisfactory method of limiting losses at the present time. Thus registration authorities have to assess the efficacy and crop safety of new pesticides in order to evaluate the benefits to be obtained from their use. These benefits have to be weighed against the potential hazards from the introduction of a new compound, the decision on granting registration incorporating this benefit/risk analysis.

The term "efficacy evaluation" is used here to cover the evaluation of pesticides for efficacy and safety to crops (and this is synonymous with the term "biological evaluation").

Registration authorities need to make use, as far as possible, of available efficacy evaluation data that may be obtained in the country or region of use, or in other countries or regions with similar climatic and agricultural conditions. Utilization of the latter data presents a number of very positive advantages, in particular:

1. the avoidance of duplication of effort, unncessary repetition of trials and consequent saving in costs and staff resources;

2. the acceleration of the registration process, permitting the more rapid utilization of effective new pesticides; and

3. the possibility of registering products for minor uses that would not justify a full trials programme in every country.

Valuable help can be found in the document, "FAO Guidelines on Efficacy Data for the Registration of Pesticides for Plant Protection" (15).

In summary, it is recommended that:

(i) Efficacy evaluation should be based primarily on the data provided by the applicant, using harmonized methods and reported in a systematically presented complete dossier;

(ii) Registration authorities should positively commit themselves to the recognition of particular internationally harmonized methods (such as the EPPO Guidelines for Biological Evaluation of Pesticides (9) (10) and to the acceptability of relevant efficacy evaluation data, produced by such methods, in other countries or regions, or from other competent sources (11) (12) (13) (14);

(iii) Where resources permit, the registration authority should participate in at least a proportion of the trials carried out by the applicant and, if deemed necessary, organize limited additional efficacy trials;

(iv) the efficacy data should, in general, contain evidence of performance of a standard pesticide with a comparable mode of action which has been included in the trials alongside the material under test;

(v) trials should be designed so as to enable the results to be subjected to statistical analysis;

(vi) petitions should contain full details of application rates, dilutions, number, timing and method of application and also descriptions of the site and the weather. Refer to FAO Guidelines on Efficacy Data for the Registration of Pesticides for Plant Protection (15).

8.3 Detailed Data on Toxicity for Assessment of Human Health Hazards

Toxicity may be defined as the inherent property or capability of a substance to cause injury when administered or absorbed by a living organism. Risk may be defined as containing two concepts: the probability that injury will result under the given conditions of use and expected exposure, sometimes referred to as hazard, and the magnitude of the resulting injury.

The assessment of risk to man and the consideration of all aspects of safety require that appropriate tests be conducted on laboratory animals as well as on biological *in vitro* systems. Such toxicological studies are designed to indicate the effects of intake through likely routes of exposure, namely oral, dermal and respiratory. It is not possible to predict with absolute precision the potential of each chemical. However, recommendations have been made to limit the inherent uncertainty of results obtained in the laboratory from tests involving biological systems. These include a minimum number of animals per sex per dose level; a wider range of dose levels; higher ceiling dosages; longer periods of treatment; use of confidence limits; and the computation of results and safety factors in extrapolation; etc., in order to minimize the statistical variation and to postulate the worst case with regard to what is likely to happen in real life.

Therefore, a well-designed and conducted assessment can provide important and reliable information on what is likely to constitute an acute human health risk, and for the estimation of the hazard of long-term dietary exposure to very low levels of pesticides or their metabolites present as residues in food. In this latter case, the use of the concept of the acceptable daily intake (ADI) by the FAO/WHO Joint Committee on Pesticide Residues is a useful example of the extrapolation of data from long-term animal feeding studies to the human dietary situation. Evaluations are based on dietary levels showing no observable adverse effect in long-term studies, to which a safety factor is added.

Implications of Risk Assessment

Valid and thorough information on toxicity is required to enable competent authorities to make decisions concerning various aspects covered by registration schemes. These include:

- possible restriction on distribution to specific groups in the community;
- labelling of the commercial formulated product with the necessary warning in accordance with an appropriate system for classifying pesticides, such as the WHO Recommended Classification of Pesticides by Hazard;
- specifying the precautions for working safety with the product before, during, and after application and establishing a safe re-entry period where appropriate;

- advising on diagnosis and treatment in case of poisoning;

- arriving at an acceptable daily intake (ADI) for man from which to judge a potential hazard from pesticide residues in or on food;

- considering the significance of pesticide residues in foods and feeds arising from the use of pesticides in accordance with good agricultural practice;

- determining what precautions are necessary to prevent harm to domestic animals, livestock and wildlife.

The toxicological studies needed to meet these objectives vary and it is not proposed to describe them in detail but rather to provide a general outline of those areas into which tests carried out under a registration scheme may fall and represent a minimum but consistent package.

Toxicological Tests - General Aspects

For each pesticide the details of the methods to be used in the investigation should be fully described and laboratory procedures should conform to a recognized code of good laboratory practice. The tests must be selected in the first instance by toxicologists in order to use the most appropriate procedures according to the chemical under study.

In view of the influence that impurities and by-products and physical state may have on toxicological properties, a detailed knowledge of the chemical and physical properties of the technical material and formulations is a necessary preliminary to any toxicological assessment procedure. The material tested should be the technical material with the same impurity pattern as the material that is intended to be registered and used.

Acute toxic hazards to applicators, by-standers and those who might be exposed during transport and storage are determined by the short-term toxicological properties of the formulated product and may not necessarily be reflected by tests done on the technical grade material. Therefore, additional acute studies conducted on the formulated material may be considered necessary. Should unusual or unexpected results be observed during the acute testing of the formulated material, additional subchronic studies may be required to try to explain these results.

Toxicological Tests:

Essential Requirements

The types of toxicological studies of pesticides which it is considered should be covered are listed below. It is a minimum set of studies necessary to evaluate properly the toxicological potential of a pesticide candidate for registration:

- acute mammalian toxicity induced by administration of a single dose, including observation of symptomatology which could provide indication of the possible mode of toxic action. The LD50 should be established and, if appropriate, the LC50, using a minimum number of animals.

  The routes of exposure should always include the oral and dermal routes. Respiratory exposure is undertaken only if indicated. The oral determination of the LD50 should be performed on both sexes of at least 2 rodent species, one of which should be rats, in order to assess possible species or sex differences. The LC50 determination through a single exposure of rats for a given period of time to an atmosphere containing the test material should only be required when the nature and the physico-chemical properties of a pesticide or its intended use pattern might create conditions which would lead to a

respiratory exposure of operators, as it is now known that the most significant route of exposure is dermal. Respiratory exposure of rats should be performed according to a recognized standard experimental protocol in view of the usual technical difficulties encountered in this type of test;

- potential irritant and corrosive properties on the skin and eye following single application; where materials are known to be corrosive these studies should be omitted.

- subchronic toxicity tests of 90-day duration. In general, the route of administration will be oral but there may be rare situations requiring sub-acute testing by other routes. Usually, these feeding studies will be performed on two species, one rodent, one non-rodent;

- reproduction studies over a minimum of two generations, usually in the rat;

- teratogenicity studies in two species, one rodent, one non-rodent;

- neurotoxicity studies in hens for organophosphorus compounds;

- mutagenicity studies covering appropriate genetic end points;

- long-term toxicity studies with administration by appropriate routes, including observations to determine the occurrence of any delayed effects and the reversibility of any lesions found. These studies should be performed in at least one species, preferably the rat;

- carcinogenicity studies. They can be combined with the long-term toxicity studies with appropriate designs;

- observation on man when feasible. This should include maintenance of health records of occupationally-exposed workers and direct observations of poisoning (clinical cases) whether accidental or deliberate. Antidotes should be recommended where possible.

Optional Tests

Some situations may require performance of additional tests or extension of tests:

- subchronic toxicity tests by routes other than oral such as repeated dermal or respiratory exposure;

- potential allergic sensitization;

- extension to other species;

- absorption, distribution and excretion studies with identification of major metabolites and metabolic pathways.

- potentiation studies are indicated whenever technical materials are intended to be later mixed in a final formulated product.

Reference may be made to OECD (19) and WHO (16) Guidelines for information on test methods.

8.4 Detailed Data on Residues in Agricultural Produce

The use of certain pesticides in accordance with good agricultural practice can result in residues in crops or livestock and, further, may leave residues in food derived therefrom. For reasons of public health, authorities should and do take the possible occurrence of residues into account in the

registration process. Many national authorities have adopted maximum residue limits (MRLs) for foods and/or feeds.

The limits, in most cases, are based on residue data required or otherwise available at the time of registration. The residue data considered by registration authorities are mostly derived from supervised trials, and it is these data that form the basis for setting MRLs.

Variations in methodologies in conducting these trials (including the selection, preparation and analysis of samples) have created difficulties in evaluating the significance of information relating to the occurrence, disappearance and fate of residues on or in crops, or groups of crops during their production, preparation for market and processing. These variations have also made it difficult to compare information from different sources and have contributed to differences in the MRLs adopted in different countries.

Although the Joint FAO/WHO Meeting on Pesticide Residues (JMPR) has provided guidance on the kind of data required for its work on the evaluation of residues in foods, the activities of those meetings and of the Codex Committee on Pesticide Residues (CCPR) have been impeded or affected by the lack of uniformity in approach to the development of data.

In response to an invitation from the ad hoc Government Consultation in 1977, CCPR through its Working Groups has developed "Guidelines on Residue Trials Methodology" and these have already been published by FAO (4), GIFAP and IUPAC (5) & (6). Further guidance on the portion of the agricultural commodity to be analysed, recommended methods of analysis and on good analytical practice in pesticide residues analysis have been prepared by CCPR (17) and also published by FAO (18).

These recommended procedures provide a basis for harmonizing the development of residue data suitable for use by national regulatory authorities both for registration purposes and for setting MRLs. Moreover, adoption of these harmonized procedures will increase transferability of data between countries, facilitate the proposal of MRLs by the JMPR and introduce consistency between the bases of data from supervised trials and surveillance data. Proposals to harmonize procedures for reporting laboratory results and for developing data for foods of animal origin are also being considered by CCPR and will be published shortly.

Information on the nature, concentration and fate of residues of the pesticide in foods and feeding stuffs, following application in accordance with proposed use directions, must form part of registration petitions. A country may decide to issue its own list of maximum residue levels (MRLs) when it has compiled sufficient evidence of the residues which are likely to occur when the pesticide is used in accordance with good agricultural practice and when the toxicological significance of these residues has been assessed. At least until such time, it is recommended that the MRL values which are recommended by the FAO/WHO Codex Alimentarius Commission (2) should be adopted. There are currently recommended limits for more than 200 pesticides, based on extensive scientific data showing the maximum residue level to be expected when crops are grown according to good agricultural practice. New pesticides and crops are continually being added to the list and it could, with benefit, be adopted as the basis of national legal limits for residues since it offers the advantage of international recognition. Refer to FAO Guidelines on Crop Residue Data (18).

8.5 Detailed Data for Prediction of Environmental Effects

The potential effects of pesticides on the environment are of great importance. Such effects must be carefully evaluated as a part of the registration process to avoid lasting damage to beneficial non-target organisms, soil, water and other important resources which could reduce the quality of life.

The risks to the environment from a pesticide are dependent on many factors, such as its toxic properties, its solubility and persistence in the environment, volatility, the amount applied, the formulation, method and time of application and particularly the extent of use. The overall effect of the pesticide also depends on the development stage of non-target species involved, the feeding habits of these species and the extent to which toxic residues or metabolic compounds may accumulate to be concentrated in successive species in food chains. The risks to wildlife may also be accentuated if the animals in the treated area are subject to some external stress; for example, by a lack of food or by adverse weather prevailing at the time.

Some pesticide effects on wildlife may be too complex, subtle, or delayed to be detected by ordinary routine testing in the laboratory or the field. It is impossible to test in such trials all the infinite variety of conditions under which the pesticide may be used in practice. Nevertheless, experience has shown that in many cases, predictions can be made of probable effects of a compound on the environment from consideration of certain basic studies.

Experience has shown that:

(a) in most cases a reasonably confident evaluation can now be made of the likely environmental effects of a pesticide product where the use pattern is known. Such an evaluation can be derived from a stepwise procedure of tests, each of which was designed to provide meaningful data;

(b) scientists have agreed on a range of basic tests designed to produce information that should be provided at the time of registration;

(c) during the early years of the registration of a product there might be a need to conduct further studies in the field to confirm predictions or indicate a need for further information.

The potential environmental effects vary greatly from country to country and situation to situation, and registration authorities should evaluate environmental risks implicit in the proposed use of a pesticide by considering the basic chemical, physical, toxicological and biological data on the product in the light of the proposed use pattern. Attention is drawn to the desirability of obtaining certain data specific to the environmental conditions after registration and an appropriate period of use, existing in the particular country or region. National authorities are urged to carry out appropriate field observations and monitoring programmes to confirm predictions or determine the need for further studies.

In deciding whether a risk is acceptable, it is of fundamental importance to consider the benefits likely to accrue from the use of the chemical. The balance between risk and benefit may differ under different socio-economic systems. Each country undertaking registration must decide what aspects of its environment might be affected by proposed pesticide use. It must also decide what values to place on these aspects and to weigh them in the light of the needs under its own agricultural and socio-economic circumstances.

In practice, information of environmental significance comes from three basic sources: application and use pattern, the fate and possible occurrence of residues in relevant parts of the environment, and the effects of predicted exposures on non-target species.

Data have to be developed prior to registration to allow a prediction to be made of the environmental behaviour of the product when applied according to the recommendations for use.

The mobility and degradation of a pesticide are of fundamental importance in the evaluation of its environmental fate. These are determined by the vapour pressure, solubility in water, partition co-efficient between water and non-miscible solvents, chemical stability and adsorption/desorption characteristics.

Assessment of the fate of a pesticide after its release into the environment may be desirable for the assessment of environmental loading and subsequent evaluation of exposure and risks from that chemical. Degradation and mobility studies are therefore the most important sources of information on the fate of a pesticide in the environment. These studies usually include analytical procedures for estimating residue levels; degradation rates and residue levels in plants, soil and water; identity of major metabolites in plants, soil and water; and leaching through soil.

Although the data on the toxicity of a pesticide used for assessing possible hazards to man are normally obtained from studies carried out with rodents, some of the results are also relevant for the prediction of potential effects on non-target species in the environment (e.g., bioaccumulation). However, since many naturally occurring organisms belong to other taxonomic groups, toxicity data on other species such as birds, aquatic invertebrates, honey bees and other beneficial arthropods form an additional part of the primary data needed for predicting potential adverse effects on non-target species. The test species should be carefully selected in order to justify broad environmental predictions being made on the basis of results from a feasible test programme. From a knowledge of the habitat of the species of concern and the sites of deposition, as well as the mobility and degradation rate of a pesticide, it is possible to estimate the exposure of the species to the pesticide.

The toxicity data available for the different organisms tested may then be used to estimate the effect of the likely exposure on related species at risk in the area. The predictive value of the basic data depends on the concept of extrapolation from one species to another. Experience has shown this to be a valid concept, although it is clearly more reliable with closely related species. By applying these considerations, it should become apparent whether particular groups of non-target species are liely to be at risk when the product is used as recommended.

In summary, it should be emphasized that:

(a) Primary data on the properties of the pesticide, fate and mobility studies, data on the toxicity of the pesticide used for assessing possible hazards to man, and information on use pattern are valuable as a means for predicting the fate of the pesticide and the effect on the environment;

(b) The main purpose of such studies is to provide data which determine the need for precautionary statements and limitations appropriate to minimize the potential adverse effects on non-target organisms; and

(c) Laboratory studies on environmental effects of pesticides which predict a pronounced positive effect against one or more test species should be checked by field studies where the many interacting environmental factors may exert their influence.

8.5.1 Evaluation of Environmental Fate and Effects

The role of the registration process is to assemble sufficient basic data to permit a reasonable prediction of environmental effects to be made.

Comprehensive guidance for those involved in the assessment and evaluation of such data is provided in FAO Guidelines on Environmental Criteria for the Registration of Pesticides (20).

In deciding whether a risk is acceptable, it is of fundamental importance to consider the benefits likely to accrue from the use of the chemical. The balance between risk and benefit may differ greatly under different socio-economic systems. Under a highly developed well-resourced system harm to rare bird species may be sufficient reason to avoid or restrict the use of a particular chemical. In situations where vector-borne human diseases, starvation or malnutrition are possible factors, the risk/benefit analysis may, however, lead to a different decision.

Thus, each country undertaking registration must decide what aspects of its environment might be affected by proposed pesticide use. It must also decide what values to place on these aspects and to weigh them in the list of its needs under its own agricultural and socio-economic circumstances.

8.5.2 Monitoring Environmental Effects

A re-evaluation of the pre-registration data is necessary if there is a substantial extension of, or change in, the use pattern. Moreover, after a pesticide has been used for some time it is desirable to confirm that the predictions about environmental effects, made at the time of registration, were valid. The absence of harmful effects is reassuring and may permit the extension of registered uses. However, doubts about the validity of the predictions indicate a need for field surveillance and monitoring studies on the occurrence of residues and on possible biological effects.

Additional laboratory and other work may be necessary. Surveillance should be made of the residue levels in the various compartments of the environment to provide information on the distribution pattern of the chemical and to identify suitable indicators for monitoring its fate and possible effects.

The biological effects of a pesticide on the environment may be assessed by monitoring changes in populations of the key indicator species, of a susceptible species or of one vulnerable because of its position in the ecosystem. Biological monitoring is also possible by assessing changes in species diversity in ecosystems or by studying physiological and behaviour parameters. The FAO Guidlines on Environmental Criteria for the Registration of Pesticides (20) contain guidance on the planning and conduct of environmental studies.

8.5.3 Post Registration Activities

If field surveillance, monitoring studies or further research give rise to doubts about the validity of predictions regarding environmental effects, the continued use or the conditions for use have to be reconsidered. Further studies on the occurrence of residues, or the possible biological effects, etc., may have

to be carried out. On the other hand, experience indicating safety in use can suggest extended use of a pesticide. Refer to FAO Guideline on Environmental Criteria for the Registration of Pesticides (20).

9. LABELLING

Labels bearing clearly legible directions for use, warnings and warning symbols in the language or languages of the country concerned should be securely fastened to each package.

In some cases illiteracy may exist in rural areas. Warning symbols should therefore receive due attention. The text should be concise, clear and logical. If it is difficult to understand, it may not even be carefully read. Label directions are especially important where cultural differences (for example in garments and footwear) may accentuate the risk of the user being exposed. In such circumstances, the label directions may need to be supplemented by special training programmes.

The main risk to the users of pesticides occurs during the handling and application procedures and particularly when the concentrated formulation is being handled prior to application. It is, therefore, most important that the labels should give sufficient information to ensure safe storage and handling, including recommended precautions to be taken when diluting and spraying the product and disposing of empty containers.

Pesticides should be applied at the correct application rate, dilution, time and frequency and by the most efficient method of application. Detailed instructions on all these matters should be set out clearly on labels. Guidelines on Good Labelling Practice for Pesticides have been developed and published by FAO (3). These should form the basis of national requirements which should be strictly enforced.

A label should be durable under practical conditions of use and handling and should, as far as possible, withstand the contents of the container or other substances with which it might be expected to come into contact. It should be easy to read and, therefore, the colour contrast of print to background, the typeface, and size of print should be chosen to achieve maximum legibility. The use of internationally agreed warning phrases and precautions, as may be recommended by FAO, is desirable. The concept of pictograms as a method of providing label instructions on safe use is under consideration. This method is not yet sufficiently advanced to recommend adoption. A draft label text and a specification for the type of paper, typeface, etc. (or preferably an example as used on another product) should form part of the registration submission.

Since the primary purpose of the pesticide label is to communicate the essential elements of the safe and effective use of the pesticide to the end use, it is essential to ensure that the audience can understand the message. Authorities should determine how much detail is necessary to achieve the desired objective of motivating the user to handle pesticides properly and to take reasonable and practical precautions when using them.

Irrespective of whether the regulatory scheme is simple or complex, new or long-established, all-embracing or restricted, the care and attention given to the consideration of the draft label is the most important and most productive feature.

Remember, the label is the main (and often, only) medium for instructing users in correct and safe use practices. The safe effective use of pesticides will ultimately depend on the user's understanding of complete, clear statements on the label, and more importantly on his ability and willingness to read and interpret this information correctly.

Full value should be taken from the FAO Guidelines on Good Labelling Practice for Pesticides (3). Failure to ensure adequate and intelligible labelling can render fruitless all other efforts to regulate pesticides.

On each and every occasion when the Pesticides Registration Director and/or the Advisory Panel have need to consider any aspect of a particular pesticide, attention should be concentrated on the label. The detailed information submitted in support of a petition for registration needs to be evaluated only insofar as it has direct bearing on the claims, uses, applications and risks indicated by the label (and any associated promotional literature). Systematic attention to this practice can greatly assist authorities in coping with the heavy work load.

9.1 Establishing Directions for Use

The directions for use will often be different from those applicable in the country of origin of the active ingredient. It is the responsibility of the applicant, either the local formulator or the importer, to propose directions suitably worded for labelling.

The elements included in the directions for use have already been mentioned in the definition of good agricultural practice. The necessary warnings and recommendations for the protection of the persons using the product should also be specified. A complication arises in that connection because safety measures, such as the wearing of impervious protective clothing, which can be observed without too much trouble in a temperate climate, may create problems in hot and humid climates. It is realistic to assume that safety instructions will often not be observed under those conditions. It may therefore be wiser not to register pesticides which would require unreasonable and unenforceable safety measures.

With regard to labelling, preference should be given to the international danger symbols, but care should be taken that any symbol used is really meaningful to the people who will handle the material.

When the directions for use have been proposed, the Pesticides Registration Director should either accept them or indicate in which respects they need to be amended. It may be useful to request the advice of specialized agricultural testing stations or similar bodies, and of public health authorities dealing with the safety of the user.

It should be clearly understood that acceptance by the Pesticides Registration Director of the directions for use should not imply acceptance of responsibility for their contents. The supplier of the goods should bear legal responsibility. In most cases, the registrar will not be in a position to bear such responsibility as he will lack the means to make independent investigations on which to base an opinion. Any attempt to do so may lead to great delays in registration, which will result in withholding new and improved pesticides from the agricultural community for perhaps a number of years.

9.2 Good Agricultural Practice

The key requirement for protection of the user is good agricultural practice, which has been defined by FAO as follows:

> "Good agricultural practice in the use of pesticides is the officially recommended or authorized usage of pesticides under practical conditions at any stage of production, storage, transport, distribution and processing of food and other agricultural commodities, and animal feed, bearing in mind the variations in requirements within and between regions which takes into account the minimum quantities necessary to achieve adequate control, applied in such a manner so as to leave a residue which is the smallest amount practicable and which is toxicologically acceptable (21)."

The officially recommended or authorized usage is that which complies with the procedures (including type of formulation, dosage rates, frequency of application and pre-harvest intervals) approved by the relevant authorities.

Good directions for use are essential to ensure conformity with the official standards of usage. Application of the directions is largely a matter of education which falls outside the scope of regulatory procedures.

9.3 Classification of Pesticides by Hazard

To assist countries to work towards the acceptance and introduction of the WHO classification of pesticides by hazard, WHO regularly issues guidelines in which pesticide active ingredients are classified (22). These are further explained in the FAO Guidelines on Good Labelling Practice for Pesticides (3). Products should be classified on the basis of data on formulations, when such data is available, in preference to extrapolating from information on active ingredients.

Where the safety of a pesticide to workers involved in its application cannot be evaluated with sufficient confidence from laboratory studies with animals, a standard protocol, "Field Survey of Exposure to Pesticides", has been developed to promote a uniform procedure where such monitoring is indicated (23).

10. PACKAGING

Products which are packed unsuitably present hazards. For example, containers which are not sufficiently robust to withstand rough handling or multi-layer stacking, or are corroded by their contents, will leak. This in itself is hazardous and can also cause contamination of other packages and can obliterate information on labels. Data on storage tests with the product in sales containers under various temperatures and relative humidities should be supplied. Predictions can be made from the results of accelerated storage tests at abnormally high temperatures, but these should be confirmed within two years of registration by tests under use conditions. Registration petitions ought to contain a full description of the proposed packages in addition to the results of storage tests. Guidelines for the Packaging and Storage of Pesticides, issued by FAO, provide a standard against which the proposed packs can be judged (24).

The quality of pesticide packages, including tamper-proof fastening and sealing, should be adequate. The packaging should not only provide protection during storage, handling and transport, but also be able to withstand adverse climatic conditions (high temperatures, humidity). Responsibility for such matters should lie with the formulator, for locally made products, or the importer, for imported goods. In addition, pesticides should only be delivered by a formulation plant or imported in sealed packages designed to be opened immediately prior to use.

11. GUIDANCE ON PRESENTATION OF REGISTRATION DATA

Uniformity in the presentation of data for registration purposes helps both the registration authorities and the petitioner in that a logical order of presentation will be easier to read and understand and there is less likelihood that evidence will be unintentionally omitted. Each registration authority should publish guidelines for manufacturers, setting out the data requirements and instructions on the method of presentation. As far as possible these requirements should be in close agreement with the recommendations in this guideline and the authorities to which reference is made in the text. Additional information, appropriate to the pesticide under consideration, should be included in the most appropriate section. All available information, published and unpublished, should be supplied. References should be given against each summary of published information.

Applications should be submitted in writing to the Pesticides Registration Authority by the manufacturer through his local representative or by the importer and should comprise a summary of all available data, prepared as described in these guidelines together with copies of any documents to which reference is made, samples of the technical grade active ingredient and formulation and copies of the proposed labels and packages. More than one copy of the summary and detailed documentation may be needed by the registration authorities.

A statement should be provided of the extent and conditions of use for which registration is requested. For example, research workers may wish to carry out small-scale trials and to use the crops for the determination of residues of the compound; at a later stage of development the petitioner may wish to market limited quantities in order to establish how the material performs under commercial conditions before finally putting it on the open market. Petitions for these various scales of use (i.e., trials, limited or full-scale, which would result in different degrees of exposure of the spray operatives, the general public and the environment) require commensurate variations in the amount of data to be supplied.

12. SITUATIONS WHERE ADDITIONAL DATA MAY BE REQUIRED

12.1 Extension of Use

In the assessment of the overall hazard of a pesticide it is necessary to know the purpose(s) for which it is sold and to have some idea of the extent of its use. During the development of the material it may be found to control additional pests or to be effective on a wider range of crops than initial trials indicated. It may also be realized that an alteration in the application rate or frequency is desirable, or that changes in the method of spraying (e.g. from high to low volume) result in improved biological control. Any such change may affect the safety of the pesticide and consequently requires a reassessment of its registration position. Therefore, a supplementary petition should be submitted giving details of extensions or alterations of the use pattern. This should contain information on the additional efficacy trials and further residue and environmental data may also be required. It should not, normally, be necessary to provide extra mammalian toxicity data if a comprehensive petition was submitted intitially, but if, for example, the use is extended to the control of aquatic weeds, extra environmental evidence should be supplied (see Section 8.5).

12.2 Formulation Changes

Post-registration changes in the nature or source of an ingredient or physical form of a pesticide product that may affect either its toxicity or its biological efficiency should be notified to the Pesticides Registration Director. Amongst the alterations liable to affect the toxicity are increases in the concentration of active ingredient or replacement of solid (e.g. granular) by liquid formulations. Efficacy also may be altered by changes in the physical form of the formulation and, in addition, by the type and quantity of the solvent(s), surface-active agents, etc. The nature and extent of additional evidence which must be supplied will depend on the formulation change and is best established by discussion with the registration authorities. It is, however, probable that the toxicity and efficacy of the new formulation will have to be determined unless the changes are very slight.

12.3 Repacking and Local Formulation

For commercial and other reasons it may be desirable to import a pesticide formulation in bulk and repack it into small containers. In such cases the original formulator, importer or the repacker should seek registration.

Application recommendations will not be helpful for the repacker, whose need is for instructions on how to handle large quantities safely. If the original manufacturer or formulator is the registrant and has agreed to the repacking, it is legitimate for the registration authorities to expect the registrant to supply drafts of labels for the repacker to print for application to smaller containers prior to sale.

The authorities should be supplied, by the repacker, with the results of storage tests in which the product was stored in the local containers; the conditions of both product and container being carefully inspected, analysed and reported. Such re-packers should be registered or licensed by the authorities to ensure compliance with "good packaging practice" and to eliminate deception or fraud.

When technical grade active ingredients or manufacturing concentrates are imported to be formulated in the importing country great care has to be exercised because of the unavailability or variability of some formulation additives (solvents, surface active agents, etc.). It is frequently impossible to reproduce exactly the product made in the country of origin and therefore the formulator should submit to the authorities, as part of the petition for registration, evidence that the toxicity, efficacy and other properties of the original formulation are relevant to the local formulation. Additives complying with the specifications of those used by the original registrant will be most likely to result in similar products, but even in these circumstances, appropriate confirmatory tests will be necessary.

12.4 Residue Levels

Experience over many years has shown that high (i.e. greater than expected) residues of pesticides in food are rare, the amounts consumed being normally well below the acceptable daily intakes established by the World Health Organization (WHO) and FAO (2). Nevertheless, regulatory authorities should exercise some control over residues in food, after the registration of a product, for the direct protection and reassurance of the consumer and to ensure the acceptability of agricultural commodities in trade.

Data on residues provided in the petition for registration will have allowed a reasonable estimate to be made of the level of residues remaining in the crop when the product has been applied according to the recommendations for use. Once the pesticide is available to be used commercially it is desirable for the competent authority to confirm that the estimate made at the time of registration is valid. To do this, samples of the produce should be taken as it leaves one or more farms where it is known that the pesticide has been used (or warehouse if a crop is treated during storage). Analyses of these samples should show if revision of the estimated maximum residue level is required.

As larger areas are treated and the use of the product is extended to additional crops, monitoring for residues may be needed to confirm whether the total residue of the pesticide in the diet is likely to exceed the acceptable daily intake. It should be remembered that considerable loss of residue is likely to occur during the post-harvest period due to food processing, preparation and cooking. However, for an assessment, rather than a prediction, of the total intake of pesticide residues by the public, dietary studies are necessary.

Guidance on producing and evaluating residue data is available in FAO Guidelines on Crop Residue Data (18).

12.5 New Evidence

Toxicological and other tests may continue even after the initial registration of a product. They may, for example be intended to clarify further the mode of action of the compound or result from a specific enquiry.

These tests, with the environmental monitoring or reports from extension officers of abnormal behaviour of a product in the field, may indicate a hazard which was not previously suspected. Therefore, results should be reported to the registration authorities if it is considered that they justify a re-assessment of the registration status.

13. HARMONIZATION OF REGISTRATION REQUIREMENTS

When considering the introduction of a registration scheme, or the expansion of an existing one, authorities should take into account the willingness to harmonize their requirements with those of other countries, expressed in Resolution XII of the ad hoc Government Consultation on Pesticides in Agriculture and Public Health, held in Rome in April 1975. It is estimated that in 1984 the development cost of a new pesticide was 15-30 million dollars and the interval between discovery of the biological activity of a compound and the first sales can be as long as 10 years. The majority of this expense and time is incurred in biological, toxicological, residue and environmental studies. A diversity of requirements by individual registration authorities can increase these costs and delays enormously and may even render it uneconomic to register a product in countries having only small potential markets.

The principle of harmonization is that the requirements for data on which to judge the suitability of a pesticide should be uniform all over the world. As all registration authorities have the same goal, namely the regulation of the use of pesticides for the protection of their people and environment, it is logical that they should seek the same type of data on which to base their judgments on the suitability of products. Similarly, assuming a stepwise approach to registration, that is, degrees of registration (trials, limited and full) commensurate with the amount of information available and the extent of the proposed use, the specific data required at the different stages should be comparable in different countries. To change a newly devised, harmonized legislation would present difficulties for countries which already have comprehensive rules for the sale and use of pesticides. However, countries without registration schemes, or where registration procedures are still very simple, have the opportunity to ensure uniformity in their request for data and thus avoid the cost of needless diversification, which could result in the exclusion of new pesticides from their country because of prohibitive registration costs.

Harmonized requirements enable countries with limited resources to take full advantage of the experience, knowledge and decisions of other countries and could be particularly advantageous in emergency situations when a country may need to register a product very quickly. Even allowing that individual governments will decide on their specific data requirements and will make their own judgment on whether to register a product, harmonization of the needs and means of measuring them will make the judgments easier, quicker and less expensive than if unique information or test methods are demanded.

13.1 Acceptability of Data

If value is to be obtained from harmonization of the requirements for registration it is necessary that, so far as possible, the data produced to meet the demands of the registration authorities are internationally accepted.

Three main categories of data are supplied for registration purposes:

1. Data obtained under controlled laboratory conditions which are valid worldwide. Provided that the protocols are acceptable and agreed following international governmental discussion and that the studies are conducted properly, the data should be accepted for evaluation by all registration authorities.

2. Data obtained under conditions which can be identified with, or related to, similar conditions or situations in other regions or countries. In the evaluation of such field test results there is need to take into account different climates and agricultural conditions but, nevertheless, properly carried out trials in a comparable region should be acceptable as evidence of performance. Likewise, residue data produced under similar geographic, climatic and ecological conditions, regardless of origin, should receive full consideration by evaluators.

3. Data which have limited value in extrapolation, i.e. data which have validity only in the local conditions under which they were obtained. Nevertheless, even these data may be of value in assessing the overall impact of a pesticide over a wide range of uses and ecological situations.

Acceptability of data depends on both suitable protocols for tests and adequate scientific standards for the conduct of them. A number of test guidelines and procedures are available (9), (10), (18) and (20).

13.2 Good Laboratory Practice

Data generated for the purpose of pesticide registration must be beyond doubt with respect to experimental design, execution of the work and final reporting. All data should be obtained in accordance with this general concept of good laboratory practice, although most currently published principles apply to health and safety data. Good laboratory practice is understood to mean that, as a minimum, the personnel involved in the supervision of the tests have the education, training and experience to carry out the work effectively; that the testing facilities and equipment are suitable and are maintained to a satisfactory standard; that the test protocol and operating procedures are observed so as to assure the Registration Authority that the work is adequately supervised and that full records of all procedures and data are kept and accurately reported. This concept has recently been given a more formal basis (GLP) but although the term is relatively new, such practices have always been used in conducting sound scientific studies. Regulatory bodies in several countries, e.g. USA, have published and introduced or intend to introduce formal guidelines on GLP. OECD has recently published principles of GLP to be applied when generating data on chemicals (25). However, in applying the principles of GLP, authorities should exercise judgment.

13.3 Proprietary Rights to Data

All data submitted by a company in support of its request for registration of its product should be treated as proprietary and should neither be divulged nor used to evaluate a petition submitted by another applicant, unless by agreement with the owner of the data or unless a period of proprietary rights to the data has expired. The synthesis of new materials and procurement of data on safety and efficacy essential for registration will have taken commercial companies many years and will have been very expensive. The results obtained are as much the property of the company that produced them as is the plant used to manufacture the product. Therefore, it would be unjust for registration authorities to use, for the benefit of industrial competitors, data submitted to them in good faith. Each applicant should be required to produce full supporting data, either by doing the work himself or by licence from the owner of the data.

Apart from the injustice of allowing competitors to benefit from the use of data to which they have no right, the consequences of such an action would be to discourage, because it is unrewarding, the research and development required for the production of new pesticides which are needed, for example, for the control of new or difficult pests or to overcome resistance.

The operating principles for proprietary rights to data are under development.

During the Second Government Consultation on International Harmonization of Pesticide Registration Requirements (Rome, 1982), GIFAP expressed the opinion that there are no objections concerning public access to health and safety data submitted in support of pesticide registrations as long as this public access does not include the right to copy that proprietary data.

14. QUALITY CONTROL

14.1 Quality of Active Ingredients

When a formulating unit imports active ingredients for further processing, a rule should be laid down to ensure that such imported materials conform to FAO or WHO specifications, if available, and that they are accompanied by a valid certificate of analysis. Where there is no FAO or WHO specification available, specifications should comply with the declaration of composition lodged at the time of registration.

14.2 Quality Control of Imported Formulated Products

In the case of imported active ingredients, the time normally available between import and further processing may be used to exercise control and carry out the necessary formalities. That interval is not always available for imported products, which may be needed on short term to deal with a threatened outbreak of pests. However, caution is necessary. When tenders are made for the supply of imported formulated products, the quality of the product must be carefully specified. Tenders have sometimes been won with bargain offers involving concessions to quality beyond acceptable limits. The following measures may offer some safeguards:

(a) the lot should be checked by a sworn sampler prior to shipping;

(b) one sample should be analysed by a reliable and well-equipped laboratory in the manufacturing country. An official body in the manufacturing country should confirm the status of the laboratory;

(c) one sample should remain in the manufacturing country and two should be sent to the receiving country. One of the latter may be used for analysis in the receiving country, and the other should be kept as a reference sample in case of a dispute;

(d) the importer should be personally responsible for ensuring compliance with the above procedures, and if the Government itself is the importer, one official should be made responsible;

(e) only on the written confirmation of the laboratory in the manufacturing country that the lot meets the required standard should the goods be released for unloading.

14.3 Methods of Quality Control

It is important that at least one official laboratory be charged with quality control of active ingredients and formulated products. Many standardized methods are available, such as those of the Collaborative International Pesticides Analytical Council (CIPAC) (26) and the Association of Official Analytical Chemists (AOAC) (27). If a certain method cannot be used because of a lack of the prescribed sophisticated instrumentation, alternative methods can often be applied with simpler equipment.

Responsible manufacturers can usually provide good descriptions of appropriate methods of analysis of their products.

15. ADDITIONAL ACTIVITIES

The wider use of a great variety of pesticides, even in remote areas, emphasizes the need to ensure that safety information reaches individual farmers and others who use the products. The text of the product label, agreed by the registration authorities, contains handling instructions, but careful reading and observance of these is unfortunately not universal. Therefore, legal powers to enforce the conditions of use may be desirable. However, such powers will need to be supplemented by local education and training in the safe and efficient use of pesticides and, therefore, provision for this should be made in a registration scheme.

Where there is a good network of extension officers, the training of farmers and others in the correct method of storing pesticides, in the choice of the most appropriate product, in application techniques and in the safe disposal of unwanted pesticides and empty containers could be part of their regular duties. Faulty applicators, particularly knapsack sprayers, are a common cause of contamination and, therefore, farmers need instruction on the maintenance and repair of spraying equipment. All possible methods of communication with the farming community should be used. They should include radio, television, films, slides, literature and posters and courses on relevant subjects. In countries where the majority of the population is involved in agriculture, there is justification for the inclusion in school and university curricula of lessons on the correct use of pesticides.

A modular course on the safe use of pesticides is available from WHO. The course is divided into more than 100 modules, each with a text and a visual aid, from which a selection, appropriate to the level and experience of the group under instruction, may be made. Films and slide collections are often available from industrial firms which, with local language commentaries, can be used for instructional purposes. Educational programmes for medical practitioners are also useful.

However carefully the precautions for the use of products are written and however clearly they appear on labels there are people who misuse commercial products, including pesticides. They may handle the concentrated material without wearing the recommended protective clothing and as a result contaminate their skin. They may apply the product incorrectly, thereby spraying themselves and their clothing. They may use household equipment, e.g., cups, as measures and leave small quantities of pesticides in them and in the unwashed product containers. They have been known to repack products into unlabelled containers or, which is even more dangerous, into containers still bearing the labels of their former contents, e.g., lemonade or fruit juice. Any of these methods of mishandling pesticides can result in poisoning necessitating medical attention. To these must be added the apparently inevitable number of those deliberately drinking pesticides in attempting suicide.

It is obviously impossible for every doctor to be aware of the symptoms and method of treatment of poisoning by all the products on the market. Some countries have established poison control centres. Registration authorities should endeavor to keep these centres informed. A doctor in a hospital emergency department presented with a case of poisoning, believed to be by a pesticide, should be able to obtain advice from the poisons centre on the diagnostic measures and on the correct treatment. This can then be started more quickly than would otherwise be the case with, consequently, a better chance of recovery.

Poisons centres should keep a record of any incidents of confirmed pesticide poisoning reported to them in order to act as one of the monitors of the safety of registered products and as an early warning of any unforeseen hazard presented by a new product. For the poisons centre to fulfil its role, it is essential that it should be kept fully up to date on new registrations and changes in product composition which may influence the toxicity of the product to humans.

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